AMENDMENTS TO THE SPECIFICATION

Please amend the title as follows:

~~SECRETED AND TRANSMEMBRANE POLYPEPTIDES AND NUCLEIC ACIDS ENCODING THE SAME~~ ANTIBODIES TO A POLYPEPTIDE ENCODED BY A NUCLEIC ACID DIFFERENTIALLY EXPRESSED IN MELANOMA

Please amend paragraph [0010] as follows:

[0010] In a further aspect, the invention concerns an isolated nucleic acid molecule comprising a nucleotide sequence having at least about 80% nucleic acid sequence identity, alternatively at least about 81% nucleic acid sequence identity, alternatively at least about 82% nucleic acid sequence identity, alternatively at least about 83% nucleic acid sequence identity, alternatively at least about 84% nucleic acid sequence identity, alternatively at least about 85% nucleic acid sequence identity, alternatively at least about 86% nucleic acid sequence identity, alternatively at least about 87% nucleic acid sequence identity, alternatively at least about 88% nucleic acid sequence identity, alternatively at least about 89% nucleic acid sequence identity, alternatively at least about 90% nucleic acid sequence identity, alternatively at least about 91% nucleic acid sequence identity, alternatively at least about 92% nucleic acid sequence identity, alternatively at least about 93% nucleic acid sequence identity, alternatively at least about 94% nucleic acid sequence identity, alternatively at least about 95% nucleic acid sequence identity, alternatively at least about 96% nucleic acid sequence identity, alternatively at least about 97% nucleic acid sequence identity, alternatively at least about 98% nucleic acid sequence identity and alternatively at least about 99% nucleic acid sequence identity to (a) a DNA molecule that encodes the same mature polypeptide encoded by any of the human protein cDNAs deposited with the ~~ATCC~~ ATCC® (American Type Culture Collection, 10801 University Blvd., Manassas, VA 20110-2209, USA) as disclosed herein, or (b) the complement of the DNA molecule of (a).

Please amend paragraph [0015] as follows:

[0015] In a further aspect, the invention concerns an isolated PRO polypeptide comprising an amino acid sequence having at least about 80% amino acid sequence identity, alternatively at least about 81% amino acid sequence identity, alternatively at least about 82% amino acid sequence identity, alternatively at least about 83% amino acid sequence identity,

alternatively at least about 84% amino acid sequence identity, alternatively at least about 85% amino acid sequence identity, alternatively at least about 86% amino acid sequence identity, alternatively at least about 87% amino acid sequence identity, alternatively at least about 88% amino acid sequence identity, alternatively at least about 89% amino acid sequence identity, alternatively at least about 90% amino acid sequence identity, alternatively at least about 91% amino acid sequence identity, alternatively at least about 92% amino acid sequence identity, alternatively at least about 93% amino acid sequence identity, alternatively at least about 94% amino acid sequence identity, alternatively at least about 95% amino acid sequence identity, alternatively at least about 96% amino acid sequence identity, alternatively at least about 97% amino acid sequence identity, alternatively at least about 98% amino acid sequence identity and alternatively at least about 99% amino acid sequence identity to an amino acid sequence encoded by any of the human protein cDNAs deposited with the ~~ATCC~~ ATCC® as disclosed herein.

Please amend paragraph [0205], beginning at page 31, as follows:

[0205] Percent amino acid sequence identity may also be determined using the sequence comparison program NCBI-BLAST2 (Altschul et al., Nucleic Acids Res. 25:3389-3402 (1997)). The NCBI-BLAST2 sequence comparison program may be downloaded from ~~http://www.ncbi.nlm.nih.gov~~ the National Institutes of Health website or otherwise obtained from the National Institute of Health, Bethesda, MD. NCBI-BLAST2 uses several search parameters, wherein all of those search parameters are set to default values including, for example, unmask = yes, strand = all, expected occurrences = 10, minimum low complexity length = 15/5, multi-pass e-value = 0.01, constant for multi-pass = 25, dropoff for final gapped alignment = 25 and scoring matrix = BLOSUM62.

Please amend paragraph [0216] beginning at page 35, as follows:

[0216] Percent nucleic acid sequence identity may also be determined using the sequence comparison program NCBI-BLAST2 (Altschul et al., Nucleic Acids Res. 25:3389-3402 (1997)). The NCBI-BLAST2 sequence comparison program may be downloaded from ~~http://www.ncbi.nlm.nih.gov~~ the National Institutes of Health website or otherwise obtained from the National Institute of Health, Bethesda, MD. NCBI-BLAST2 uses several search

parameters, wherein all of those search parameters are set to default values including, for example, unmask = yes, strand = all, expected occurrences = 10, minimum low complexity length = 15/5, multi-pass e-value = 0.01, constant for multi-pass = 25, dropoff for final gapped alignment = 25 and scoring matrix = BLOSUM62.—

Please amend paragraph [0237], beginning at page 40, as follows:

[0237] "Carriers" as used herein include pharmaceutically acceptable carriers, excipients, or stabilizers which are nontoxic to the cell or mammal being exposed thereto at the dosages and concentrations employed. Often the physiologically acceptable carrier is an aqueous pH buffered solution. Examples of physiologically acceptable carriers include buffers such as phosphate, citrate, and other organic acids; antioxidants including ascorbic acid; low molecular weight (less than about 10 residues) polypeptide; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids such as glycine, glutamine, asparagine, arginine or lysine; monosaccharides, disaccharides, and other carbohydrates including glucose, mannose, or dextrins; chelating agents such as EDTA; sugar alcohols such as mannitol or sorbitol; salt-forming counterions such as sodium; and/or nonionic surfactants such as TWEEN™ (a polyoxyethylene (20) sorbitan available from ICI Americas, Inc., Bridgewater, NJ), polyethylene glycol (PEG), and PLURONICS™ (a copolymer of propylene oxide and ethylene oxide available from BASF Corporation, Mount Olive, NJ).

Please amend paragraph [0255] as follows:

[0255] As disclosed in the Examples below, various cDNA clones have been deposited with the ~~ATCC~~ ATCC®. The actual nucleotide sequences of those clones can readily be determined by the skilled artisan by sequencing of the deposited clone using routine methods in the art. The predicted amino acid sequence can be determined from the nucleotide sequence using routine skill. For the PRO polypeptides and encoding nucleic acids described herein, Applicants have identified what is believed to be the reading frame best identifiable with the sequence information available at the time.

Please amend paragraph [0294] as follows:

[0294] Suitable host cells for cloning or expressing the DNA in the vectors herein include prokaryote, yeast, or higher eukaryote cells. Suitable prokaryotes include but are not limited to eubacteria, such as Gram-negative or Gram-positive organisms, for example, Enterobacteriaceae such as *E. coli*. Various *E. coli* strains are publicly available, such as *E. coli* K12 strain MM294 (~~ATCC~~ ATCC® 31,446); *E. coli* X1776 (~~ATCC~~ ATCC® 31,537); *E. coli* strain W3110 (~~ATCC~~ ATCC® 27,325) and K5 772 (~~ATCC~~ ATCC® 53,635). Other suitable prokaryotic host cells include Enterobacteriaceae such as *Escherichia*, e.g., *E. coli*, *Enterobacter*, *Erwinia*, *Klebsiella*, *Proteus*, *Salmonella*, e.g., *Salmonella* typhimurium, *Serratia*, e.g., *Serratia marcescans*, and *Shigella*, as well as *Bacilli* such as *B. subtilis* and *B. licheniformis* (e.g., *B. licheniformis* 41P disclosed in DD 266,710 published 12 April 1989), *Pseudomonas* such as *P. aeruginosa*, and *Streptomyces*. These examples are illustrative rather than limiting. Strain W3110 is one particularly preferred host or parent host because it is a common host strain for recombinant DNA product fermentations. Preferably, the host cell secretes minimal amounts of proteolytic enzymes. For example, strain W3110 may be modified to effect a genetic mutation in the genes encoding proteins endogenous to the host, with examples of such hosts including *E. coli* W3110 strain 1A2, which has the complete genotype *tonA* ; *E. coli* W3110 strain 9E4, which has the complete genotype *tonA ptr3*; *E. coli* W3110 strain 27C7 (~~ATCC~~ ATCC® 55,244), which has the complete genotype *tonA ptr3 phoA E15 (argF-lac)169 degP ompT kan*^{r}; *E. coli* W3110 strain 37D6, which has the complete genotype *tonA ptr3 phoA E15 (argF-lac)169 degP ompT rbs7 ilvG kan*^{r}; *E. coli* W3110 strain 40B4, which is strain 37D6 with a non-kanamycin resistant *degP* deletion mutation; and an *E. coli* strain having mutant periplasmic protease disclosed in U.S. Patent No. 4,946,783 issued 7 August 1990. Alternatively, *in vitro* methods of cloning, e.g., PCR or other nucleic acid polymerase reactions, are suitable.

Please amend paragraph [0295] as follows:

[0295] In addition to prokaryotes, eukaryotic microbes such as filamentous fungi or yeast are suitable cloning or expression hosts for PRO-encoding vectors. *Saccharomyces cerevisiae* is a commonly used lower eukaryotic host microorganism. Others include *Schizosaccharomyces pombe* (Beach and Nurse, Nature, 290: 140 [1981]; EP 139,383 published

2 May 1985); *Kluyveromyces* hosts (U.S. Patent No. 4,943,529; Fleer et al., Bio/Technology, 9:968-975 (1991)) such as, e.g., *K. lactis* (MW98-8C, CBS683, CBS4574; Louvencourt et al., J. Bacteriol., 154(2):737-742 [1983]), *K. fragilis* (~~ATCC~~ ATCC® 12,424), *K. bulgaricus* (~~ATCC~~ ATCC® 16,045), *K. wickeramii* (~~ATCC~~ ATCC® 24,178), *K. waltii* (~~ATCC~~ ATCC® 56,500), *K. drosophilarum* (~~ATCC~~ ATCC® 36,906; Van den Berg et al., Bio/Technology, 8:135 (1990)), *K. thermotolerans*, and *K. marxianus; yarrowia* (EP 402,226); *Pichia pastoris* (EP 183,070; Sreekrishna et al., J. Basic Microbiol., 28:265-278 [1988]); *Candida; Trichoderma reesia* (EP 244,234); *Neurospora crassa* (Case et al., Proc. Natl. Acad. Sci. USA, 76:5259-5263 [1979]); *Schwanniomyces* such as *Schwanniomyces occidentalis* (EP 394,538 published 31 October 1990); and filamentous fungi such as, e.g., *Neurospora, Penicillium, Tolypocladium* (WO 91/00357 published 10 January 1991), and *Aspergillus* hosts such as *A. nidulans* (Ballance et al., Biochem. Biophys. Res. Commun., 112:284-289 [1983]; Tilburn et al., Gene, 26:205-221 [1983]; Yelton et al., Proc. Natl. Acad. Sci. USA, 81: 1470-1474 [1984]) and *A. niger* (Kelly and Hynes, EMBO J., 4:475-479 [1985]). Methylotropic yeasts are suitable herein and include, but are not limited to, yeast capable of growth on methanol selected from the genera consisting of *Hansenula, Candida, Kloeckera, Pichia, Saccharomyces, Torulopsis,* and *Rhodotorula.* A list of specific species that are exemplary of this class of yeasts may be found in C. Anthony, The Biochemistry of Methylotrophs, 269 (1982).

Please amend paragraph [0296] as follows:

[0296] Suitable host cells for the expression of glycosylated PRO are derived from multicellular organisms. Examples of invertebrate cells include insect cells such as Drosophila S2 and Spodoptera Sf9, as well as plant cells. Examples of useful mammalian host cell lines include Chinese hamster ovary (CHO) and COS cells. More specific examples include monkey kidney CV1 line transformed by SV40 (COS-7, ~~ATCC~~ ATCC® CRL 1651); human embryonic kidney line (293 or 293 cells subcloned for growth in suspension culture, Graham et al., J. Gen Virol., 36:59 (1977)); Chinese hamster ovary cells/-DHFR (CHO, Urlaub and Chasin, Proc. Natl. Acad. Sci. USA, 77:4216 (1980)); mouse sertoli cells (TM4, Mather, Biol. Reprod., 23:243-251 (1980)); human lung cells (W138, ~~ATCC~~ ATCC® CCL 75); human liver cells (Hep G2, HB

8065); and mouse mammary tumor (MMT 060562, ~~ATCC~~ ATCC® CCL51). The selection of the appropriate host cell is deemed to be within the skill in the art.

Please amend paragraph [0302] as follows:

[0302] An example of suitable selectable markers for mammalian cells are those that enable the identification of cells competent to take up the PRO-encoding nucleic acid, such as DHFR or thymidine kinase. An appropriate host cell when wild-type DHFR is employed is the CHO cell line deficient in DHFR activity, prepared and propagated as described by Urlaub et al., Proc. Natl. Acad. Sci. USA, 77:4216 (1980). A suitable selection gene for use in yeast is the *trp*1 gene present in the yeast plasmid YRp7 [Stinchcomb et al., Nature, 282:39 (1979); Kingsman et al., Gene, 7:141 (1979); Tschemper et al., Gene, 10:157 (1980)]. The *trp*1 gene provides a selection marker for a mutant strain of yeast lacking the ability to grow in tryptophan, for example, ~~ATCC~~ ATCC® No. 44076 or PEP4-1 [Jones, Genetics, 85:12 (1977)].

Please amend paragraph [337], beginning at page 93, as follows:

[0337] The PRO polypeptides described herein may also be employed as therapeutic agents. The PRO polypeptides of the present invention can be formulated according to known methods to prepare pharmaceutically useful compositions, whereby the PRO product hereof is combined in admixture with a pharmaceutically acceptable carrier vehicle. Therapeutic formulations are prepared for storage by mixing the active ingredient having the desired degree of purity with optional physiologically acceptable carriers, excipients or stabilizers (Remington's Pharmaceutical Sciences 16th edition, Osol, A. Ed. (1980)), in the form of lyophilized formulations or aqueous solutions. Acceptable carriers, excipients or stabilizers are nontoxic to recipients at the dosages and concentrations employed, and include buffers such as phosphate, citrate, and other organic acids; antioxidants including ascorbic acid; low molecular weight (less than about 10 residues) polypeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids such as glycine, glutamine, asparagine, arginine or lysine; monosaccharides, disaccharides and other carbohydrates including glucose, mannose, or dextrins; chelating agents such as EDTA; sugar alcohols such as mannitol or sorbitol; salt-forming counterions such as sodium; and/or nonionic

surfactants such as TWEEN™ (a polyoxyethylene (20) sorbitan available from ICI Americas, Inc., Bridgewater, NJ), PLURONICS™ (a copolymer of propylene oxide and ethylene oxide available from BASF Corporation, Mount Olive, NJ) or PEG (polyethylene glycol).

Please amend paragraph [0405], beginning at page 111, as follows:

[0405] Sustained-release preparations may be prepared. Suitable examples of sustained-release preparations include semipermeable matrices of solid hydrophobic polymers containing the antibody, which matrices are in the form of shaped articles, *e.g.*, films, or microcapsules. Examples of sustained-release matrices include polyesters, hydrogels (for example, poly(2-hydroxyethyl-methacrylate), or poly(vinylalcohol)), polylactides (U.S. Pat. No. 3,773,919), copolymers of L-glutamic acid and γ ethyl-L-glutamate, non-degradable ethylene-vinyl acetate, degradable lactic acid-glycolic acid copolymers such as LUPRON DEPOT™ (injectable microspheres composed of lactic acid-glycolic acid copolymer and leuprolide acetate) (TAP Pharmaceuticals, Inc., Chicago, IL), and poly-D-(-)-3-hydroxybutyric acid. While polymers such as ethylene-vinyl acetate and lactic acid-glycolic acid enable release of molecules for over 100 days, certain hydrogels release proteins for shorter time periods. When encapsulated antibodies remain in the body for a long time, they may denature or aggregate as a result of exposure to moisture at 37° C, resulting in a loss of biological activity and possible changes in immunogenicity. Rational strategies can be devised for stabilization depending on the mechanism involved. For example, if the aggregation mechanism is discovered to be intermolecular S-S bond formation through thio-disulfide interchange, stablization may be achieved by modifying sulfhydryl residues, lyophilizing from acidic solutions, controlling moisture content, using appropriate additives, and developing specific polymer matrix compositions.

Please amend paragraph [0412] as follows:

[0412] Commercially available reagents referred to in the examples were used according to manufacturer's instructions unless otherwise indicated. The source of those cells identified in the following examples, and throughout the specification, by ~~ATCC~~ ATCC® accession numbers is the American Type Culture Collection, Manassas, VA.

Please amend paragraph [0426] as follows:

[0426] The yeast strain used was HD56-5A (~~ATCC~~ ATCC®-90785). This strain has the following genotype: MAT alpha, ura3-52, leu2-3, leu2-112, his3-11, his3-15, MAL^+, SUC^+, GAL^+. Preferably, yeast mutants can be employed that have deficient post-translational pathways. Such mutants may have translocation deficient alleles in *sec*71, *sec*72, *sec*62, with truncated *sec*71 being most preferred. Alternatively, antagonists (including antisense nucleotides and/or ligands) which interfere with the normal operation of these genes, other proteins implicated in this post translation pathway (e.g., SEC61p, SEC72p, SEC62p, SEC63p, TDJ1p or SSA1p-4p) or the complex formation of these proteins may also be preferably employed in combination with the amylase-expressing yeast.

Please amend paragraph [0435], beginning at page 117, as follows:

[0435] When a positive colony was isolated, a portion of it was picked by a toothpick and diluted into sterile water (30 µl) in a 96 well plate. At this time, the positive colonies were either frozen and stored for subsequent analysis or immediately amplified. An aliquot of cells (5 µl) was used as a template for the PCR reaction in a 25 µl volume containing: 0.5 µl ~~Klentaq~~ KLENTAQ (a 5'-exo minus N-terminal deletion of Taq DNA polymerase available from Clontech, Palo Alto, CA); 4.0 µl 10 mM dNTP's (Perkin Elmer-Cetus); 2.5 µl ~~Klentaq~~ KLENTAQ buffer (Clontech); 0.25 µl forward oligo 1; 0.25 µl reverse oligo 2; 12.5 µl distilled water. The sequence of the forward oligonucleotide 1 was:

Please amend paragraph [0441], on page 119, as follows:

[0441] Following the PCR, an aliquot of the reaction (5 µl) was examined by agarose gel electrophoresis in a 1% agarose gel using a Tris-Borate-EDTA (TBE) buffering system as described by Sambrook et al., supra. Clones resulting in a single strong PCR product larger than 400 bp were further analyzed by DNA sequencing after purification with a 96 ~~Qiaquick~~ QIAQUICK PCR clean-up column (Qiagen Inc., Chatsworth, CA).

Please amend paragraph [0445] as follows:

[0445] Using the techniques described in Examples 1 to 3 above, numerous full-length cDNA clones were identified as encoding PRO polypeptides as disclosed herein. These cDNAs were then deposited under the terms of the Budapest Treaty with the American Type Culture Collection, 10801 University Blvd., Manassas, VA 20110-2209, USA (~~ATCC~~ ATCC®) as shown in Table 7 below.

Please replace Table 7 with the following table:

Table 7

Material	~~ATCC~~ ATCC® Dep. No.	Deposit Date
DNA26843-1389	203099	August 4, 1998
DNA30867-1335	209807	April 28, 1998
DNA34431-1177	209399	October 17, 1997
DNA38268-1188	209421	October 28, 1997
DNA40621-1440	209922	June 2, 1998
DNA40625-1189	209788	April 21, 1998
DNA45409-2511	203579	January 12, 1999
DNA45495-1550	203156	August 25, 1998
DNA49820-1427	209932	June 2, 1998
DNA56406-1704	203478	November 17, 1998
DNA56410-1414	209923	June 2, 1998
DNA56436-1448	209902	May 27, 1998
DNA56855-1447	203004	June 23, 1998
DNA56860-1510	209952	June 9, 1998
DNA56862-1343	203174	September 1, 1998
DNA56868-1478	203024	June 23, 1998
DNA56869-1545	203161	August 25, 1998
DNA57704-1452	209953	June 9, 1998
DNA58723-1588	203133	August 18, 1998
DNA57827-1493	203045	July 1, 1998
DNA58737-1473	203136	August 18, 1998
DNA58846-1409	209957	June 9, 1998
DNA58850-1495	209956	June 9, 1998
DNA58855-1422	203018	June 23, 1998
DNA59211-1450	209960	June 9, 1998
DNA59212-1627	203245	September 9, 1998
DNA59213-1487	209959	June 9, 1998
DNA59605-1418	203005	June 23, 1998
DNA59609-1470	209963	June 9, 1998
DNA59610-1556	209990	June 16, 1998
DNA59837-2545	203658	February 9, 1999

DNA59844-2542	203650	February 9, 1999
DNA59854-1459	209974	June 16, 1998
DNA60625-1507	209975	June 16, 1998
DNA60629-1481	209979	June 16, 1998
DNA61755-1554	203112	August 11, 1998
DNA62812-1594	203248	September 9, 1998
DNA62815-1576	203247	September 9, 1998
DNA64881-1602	203240	September 9, 1998
DNA64886-1601	203241	September 9, 1998
DNA64902-1667	203317	October 6, 1998
DNA64950-1590	203224	September 15, 1998
DNA65403-1565	203230	September 15, 1998
DNA66308-1537	203159	August 25, 1998
DNA66519-1535	203236	September 15, 1998
DNA66521-1583	203225	September 15, 1998
DNA66658-1584	203229	September 15, 1998
DNA66660-1585	203279	September 22, 1998
DNA66663-1598	203268	September 22, 1998
DNA66674-1599	203281	September 22, 1998
DNA68862-2546	203652	February 9, 1999
DNA68866-1644	203283	September 22, 1998
DNA68871-1638	203280	September 22, 1998
DNA68880-1676	203319	October 6, 1998
DNA68883-1691	203535	December 15, 1998
DNA68885-1678	203311	October 6, 1998
DNA71277-1636	203285	September 22, 1998
DNA73727-1673	203459	November 3, 1998
DNA73734-1680	203363	October 20, 1998
DNA73735-1681	203356	October 20, 1998
DNA76393-1664	203323	October 6, 1998
DNA77301-1708	203407	October 27, 1998
DNA77568-1626	203134	August 18, 1998
DNA77626-1705	203536	December 15, 1998
DNA81754-2532	203542	December 15, 1998
DNA81757-2512	203543	December 15, 1998
DNA82302-2529	203534	December 15, 1998
DNA82340-2530	203547	December 22, 1998
DNA83500-2506	203391	October 29, 1998
DNA84920-2614	203966	April 27, 1999
DNA85066-2534	203588	January 12, 1999
DNA86571-2551	203660	February 9, 1999
DNA87991-2540	203656	February 9, 1999
DNA92238-2539	203602	January 20, 1999
DNA96042-2682	PTA-382	July 20, 1999
DNA96787-2534	203589	January 12, 1999

DNA125185-2806	PTA-1031	December 7, 1999
DNA147531-2821	PTA-1185	January 11, 2000
DNA115291-2681	PTA-202	June 8, 1999
DNA164625-28890	PTA-1535	March 21, 2000
DNA131639-2874	PTA-1784	April 25, 2000
DNA79230-2525	203549	December 22, 1998

Please amend paragraph [0446], on page 122-123, as follows:

[0446] These deposits were made under the provisions of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure and the Regulations thereunder (Budapest Treaty). This assures maintenance of a viable culture of the deposit for 30 years from the date of deposit and at least 5 years after the most recent request for the furnishing of a sample of the deposit was received by the depository. The deposits will be made available by ATCC under the terms of theBudapest Treaty, and subject to an agreement between Genentech, Inc. and ATCC, which assures permanent and unrestricted availability of the progeny of the culture of the deposit to the public upon issuance of the pertinent U.S. patent or upon laying open to the public of any U.S. or foreign patent application, whichever comes first, and assures availability of the progeny to one determined by the U.S. Commissioner of Patents and Trademarks to be entitled thereto according to 35 USC § 122 and the Commissioner's rules pursuant thereto (including 37 CFR § 1.14. with particular reference to 886 OG 638).

Please amend paragraph [0467] as follows:

[0467] In one embodiment, the selected host cells may be 293 cells. Human 293 cells (~~ATCC~~ ATCC® CCL 1573) are grown to confluence in tissue culture plates in medium such as DMEM supplemented with fetal calf serum and optionally, nutrient components and/or antibiotics. About 10 μg pRK5-PRO DNA is mixed with about 1 μg DNA encoding the VA RNA gene [Thimmappaya et al., Cell, 31:543 (1982)] and dissolved in 500 μl of 1 mM Tris-HCl, 0.1 mM EDTA, 0.227 M $CaCl_2$. To this mixture is added, dropwise, 500 μl of 50 mM HEPES (pH 7.35), 280 mM NaCl, 1.5 mM $NaPO_4$, and a precipitate is allowed to form for 10 minutes at 25°C. The precipitate is suspended and added to the 293 cells and allowed to settle for about

four hours at 37°C. The culture medium is aspirated off and 2 ml of 20% glycerol in PBS is added for 30 seconds. The 293 cells are then washed with serum free medium, fresh medium is added and the cells are incubated for about 5 days.

Please amend paragraph [0475], beginning on page 129 as follows:

[0475] Twelve micrograms of the desired plasmid DNA is introduced into approximately 10 million CHO cells using commercially available transfection reagents ~~Superfect™ (Quiagen)~~ SUPERFECT™ (Qiagen), ~~dosper™~~ DOSPER™ or ~~fugene™~~ FUGENE™ (Boehringer Mannheim). The cells are grown as described in Lucas et al., supra. Approximately 3×10^{-7} cells are frozen in an ampule for further growth and production as described below.

Please amend paragraph [0489] beginning on page 131 as follows:

[0489] Recombinant baculovirus is generated by co-transfecting the above plasmid and ~~BaculoGold™~~ BACULOGOLD™ virus DNA (Pharmingen) into *Spodoptera frugiperda* ("Sf9") cells ((~~ATCC~~ ATCC® CRL 1711) using ~~lipofectin~~ LIPOFECTIN cationic lipid (commercially available from GIBCO-BRL). After 4 - 5 days of incubation at 58°C, the released viruses are harvested and used for further amplifications. Viral infection and protein expression are performed as described by O'Reilley et al., Baculovirus expression vectors: A Laboratory Manual, Oxford: Oxford University Press (1994).

Please amend paragraph [0497] as follows:

[0497] After a suitable antibody titer has been detected, the animals "positive" for antibodies can be injected with a final intravenous injection of PRO. Three to four days later, the mice are sacrificed and the spleen cells are harvested. The spleen cells are then fused (using 35% polyethylene glycol) to a selected murine myeloma cell line such as P3X63AgU.1, available from ~~ATCC~~ ATCC®, No. CRL 1597. The fusions generate hybridoma cells which can then be plated in 96 well tissue culture plates containing HAT (hypoxanthine, aminopterin, and thymidine) medium to inhibit proliferation of non-fused cells, myeloma hybrids, and spleen cell hybrids.